Examiner alleged that claims 26-28, 37, 56, and 61-63 were drawn to a method for detecting the "absence" of neoplastic cells having an increased copy of number of nucleic acid sequences at chromosome region 20q13.2 and argued that the specification does not contemplate a method of detecting the absence of neoplastic cells. Applicants traverse by argument and amendment.

Applicants note that the Examiner appears to recognize that the specification discloses a method of detecting the **presence** of neoplastic cells having an increased copy of number of nucleic acid sequences at chromosome region 20q13.2. Moreover one of ordinary skill would readily recognize that **where an assay that detects the presence of a particular target (*e.g.* amplifications at chromosome region 20q13.2) fails to detect such the target, the assay has implicitly detected the absence of that target**. Thus, the specification clearly provides a method for detecting the absence of the recited neoplastic cells. Accordingly, the rejection under 35 U.S.C. §112, first paragraph, new matter grounds should be withdrawn.

35 U.S.C. §112, Second Paragraph.

Claims 26-28, 37, 56, and 61-63 were rejected as allegedly indefinite for the use of the language "relative" in claim 26. The Examiner alleged that "[i]t is not clear the copy number is relative to what.". Applicants respectfully traverse.

The term "relative copy number" is a term of art well known to those of skill in the art (*see* http://www.helsinki.fi/biochipcenter/technology.htm (biochip technology overview), paragraph on CGH Microarrays). The term indicates simply that the measurement, while quantitative need not be an **absolute** measure of copy number (*i.e.* one copy, two copies, three copies, four copies, *etc.*).

The term clearly "apprise[s] those skilled in the art both of the utilization and scope of the invention" and is "as precise as the subject matter permits." *See, In re Jackson*, 217 USPQ. 804, 806 (BPAI, 1982). Accordingly, 26-28, 37, 56, and 61-63 meet the requirements of 35 U.S.S. §112, second paragraph, and the rejection on these grounds should be withdrawn.

35 U.S.C. §112, First Paragraph, Written Description.

Claims 26 and 37 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking a clear written description. In particular, the Examiner alleged that numerous unrelated sequences that partially hybridize under the recited stringent conditions with the claimed nucleotide sequence would be detected. Applicants respectfully traverse.

The Examiner's rejection is not properly a "written description" rejection.

The Examiner is reminded that "the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. [emphasis added] '" *Union Oil Co. v Atlantic Richfield et al.* 208 F.3d 989 (Fed. Cir. 2000) *citing In re Gosteli*, 872 F.2d 1008, 1012, 10 U.S.P.Q.2D (BNA) 1614, 1618 (Fed. Cir. 1989).

In the present case, independent claim 26 expressly recites:

> [C]ontacting a nucleic acid sample from a human patient with a probe which **hybridizes to a target polynucleotide sequence under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes, the target polynucleotide sequence comprising a sequence selected from the group consisting of** SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, **SEQ ID NO:9**, . . . [emphasis added]

There is simply no question that the specification, as filed, communicates to one of ordinary skill in the art that Applicants were in possession of:

> [A] probe **which hybridizes to a target polynucleotide sequence under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes, the target polynucleotide sequence comprising a sequence selected from the group consisting of** SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, **SEQ ID NO:9.**

The Examiner's allegation that "numerous unrelated sequences that partially hybridize under the recited stringent conditions with the claimed nucleotide sequence would be detected" is a statement that the Examiner doesn't believe the claimed method would permit detection of amplifications at 20q13.2 and is the substance of a "make and use" enablement rejection, not "written description".

Moreover, the Examiner has offered no objective evidence to support here assertion that "numerous unrelated sequences that partially hybridize under the recited stringent conditions with the claimed nucleotide sequence would be detected". Indeed, the Examiner has failed to establish that a such sequences would be present in the assay.

Accordingly, the Examiner has failed to make a *prima facie* case under 35 U.S.C. §112, first paragraph, and the rejection on written description or enablement grounds should be withdrwn.

35 U.S.C. §112, First Paragraph, Enablement.

Claims 26-28, 37, 56, and 61-63 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to enable one of skill in the art to make or use the invention. In particular, the Examiner alleged that the specification is not enabling "for a method for detecting **any** neoplastic cells". [emphasis added] (See Office Action, page 4, lines 7-9). Applicants traverse.

In making her rejection, the Examiner implicitly reads a limitation into the claims that is not present. In particular, the Examiner states:

> The Examiner reads the claims broadly, but within reasonable interpretation. The breadth of the claims encopmpasses a method for detectin "**any neoplastic cells**", having an increase copy number of "**any nucleic acid** sequence" at chromosomal region 20q13.2. . . [emphnasis added] (Office Action, page 5, lines 6-9)

Claim 26, however expressly recites:

> 26. A method of detecting in a sample the presence or absence of **neoplastic cells having an increased copy number of nucleic acid sequences at chromosome region 20q13.2**, the method comprising:
>
> contacting a nucleic acid sample from a human patient with a probe that fully hybridizes to a target polynucleotide sequence under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes, the target polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and SEQ ID NO:13 wherein the probe is contacted with the sample under conditions in which the probe hybridizes selectively with the target polynucleotide sequence to form a stable hybridization complex; and
>
> detecting the formation of a hybridization complex to determine the relative copy number of a nucleic acid in chromosomal region 20q13.2, thereby identifying the presence or absence of neoplastic cells having an increased copy number of nucleic acid sequences at chromosomal region 20q13.2. [emphasis added]

Applicants respectfully invite the Examiner to identify with particularity (*i.e.* by reference to line number) where the aforementioned language, "**any neoplastic cells**" or "**any nucleic acid**" is found in claim 26. The language identified by the Examiner and forming the basis of her rejection simply does not exist in the pending claims.

To the contrary, the claim merely recites "a method of detecting in a sample the presence or absence of neoplastic cells. . .". The language is clear on its face. It **does not** refer to "**any** neoplastic cells" or to "**all** neoplastic cells".

To the contrary, the claim is directed to detecting the presence or absence of **neoplastic cells having an increased copy number of nucleic acid sequences at chromosome region 20q13.2**.

No undue experimentation is required to practice the presently claimed invention. All one need do is perform the claimed assay steps (*e.g.* as exemplified in the specification). If the assay provides a positive result (*i.e.* using the probes recited in the claim), that indicates the presence **neoplastic cells having an increased copy number of nucleic acid sequences at chromosome region 20q13.2** in the subject sample.

The fact that genes other than those identified in the present claims may also be amplified at 20q13.2 in neoplastic cells is simply irrelevant to enablement of the presently claimed invention. As explained above, the claim is not directed to the detection of any nucleic acid or to all amplifications at 20q13.2. That the G-s-alpha subunit gene, allegedly mapped to the chromosomal region 201q13.2 and allegedly having increased levels in peripheral leuckocytes of manic patients is according to the Examiner unrelated to the claims SEQ ID NO:9, **does not mitigate the efficacy of probes to SEQ ID NO:9, to identify amplifications at 20q13.2.**

The Examiner does not dispute the efficacy of the recited probes for identifying amplifications at 20q13.2 or the association of such amplifications with neoplastic cells. The Examiner has provided no objective basis to support an allegation that performing the presently claimed method will fail to identify amplifications at 20q13.2 in a sample containing cells having such amplifications.

That there may exist amplifications that are not detected by the claimed method simply does not negative the operability of that method. Once again, as indicated above, the method does not purport to identify all cells having such an amplification.

The Examiner's rejection under 35 U.S.C. §112, first paragraph, is thus premised reading a limitation ("any nucleic acid") into the claim. As explained above, this limitation is not present. Moreover, it simply does not require undue experimentation to perform the steps recited in the claim and the Examiner has failed to establish that the claimed method is ineffective for detecting amplifications at 20q13.2. Consequently, the Examiner has failed to establish that the claimed method is ineffective or that practicing the recited steps would require undue experimentation. Accordingly, the Examiner has

failed to make her *prima facie* case, and the rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

35 U.S.C. §112, first paragraph, scope.

Claims 26-28, 37, 56, and 61-63 were rejected under 35 U.S.C. §112, first paragraph, as allegedly overbroad because the specification is allegedly not enabling for a method "for detecting in 'any sample' the presence of neoplastic cells having an increased copy number . . . " (Office Action page 7, lines 1-2). In particular, the Examiner states

> It is not clear how one could detect the prsenceof neoplastic cells having an increased copy number of nuclic acid sequences at chromosome region 201q13.2, using any sample, for example normal tissues, even from a patient with breast cancer. . .

Applicants respectfully submit that the Examiner fails to accurately note all of the limitation of the pending claims. The preamble of claim 26, for example reads:

> 26. A method of detecting in a sample **the presence or absence** of neoplastic cells having an increased copy number of nucleic acid sequences at chromosome region 20q13.2,

In a sample **lacking** neoplastic cells with an amplification at 20q13.2, the assay will be **negative**, *i.e.,* the assay will report the **absence** of neoplastic cells in the subject sample as recited in the preamble of the claim.

The scope of the pending claims is thus fully commensurate with the Applicant's invention and no undue experimentation is required to practice the presently claimed methods.

Accordingly, the rejection of claims 26-28, 37, 56, and 61-63 35 U.S.C. §112, first paragraph, on "scope" grounds should be withdrawn.

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner still maintains any of the foregoing rejections in view of this response, Applicants request a telephone interview to discuss the matter.

QUINE INTELLECTUAL PROPERTY LAW
GROUP, P.C.
P.O. BOX 458
Alameda, CA 94501
Tel: 510 337-7871
Fax: 510 337-7877

Respectfully submitted,

Tom Hunter
Reg. No: 38,498

c:\toms work_amendments\407t uc ott\407t-895720us\407t-895720us.am4.doc

APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE IN 08/785,532 WITH ENTRY OF THIS AMENDMENT

In the specification:

No amendments.

In the claims:

No amendments.

APPENDIX B

CLAIMS PENDING IN USSN 08/785,532 WITH ENTRY OF THIS AMENDMENT

26. A method of detecting in a sample the presence or absence of neoplastic cells having an increased copy number of nucleic acid sequences at chromosome region 20q13.2, the method comprising:

contacting a nucleic acid sample from a human patient with a probe which hybridizes to a target polynucleotide sequence under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes, the target polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and SEQ ID NO:13 wherein the probe is contacted with the sample under conditions in which the probe hybridizes selectively with the target polynucleotide sequence to form a stable hybridization complex; and

detecting the formation of a hybridization complex to determine the relative copy number of a nucleic acid in chromosomal region 20q13.2, thereby identifying the presence or absence of neoplastic cells having an increased copy number of nucleic acid sequences at chromosomal region 20q13.2.

27. The method of claim 26, wherein the nucleic acid sample is from a patient with breast cancer.

28. The method of claim 26, wherein the nucleic acid sample is a metaphase spread or a interphase nucleus.

29. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:1.

30. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:2.

31. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:3.

32. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:4.

33. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:5.

34. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:6.

35. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:7.

36. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:8.

37. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:9.

38. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:10.

39. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:12.

40. The method of claim 26, wherein the probe comprises a polynucleotide sequence as set forth in SEQ ID NO:45.

48. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:1 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

49. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:2 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

50. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:3 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

51. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:4 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

52. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:5 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

53. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:6 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

54. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:7 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

55. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:8 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

56. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:9 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

57. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:10 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

58. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:11 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

59. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:12 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

60. The method of claim 26, wherein the probe comprises a polynucleotide sequence that hybridizes to SEQ ID NO:45 under stringent conditions that include washing with 0.2x SSC at 65°C for 15 minutes.

61. The method of claim 26, wherein the probe is labeled.

62. The method of claim 61, wherein the label is a fluorescent label.

63. The method of claim 26, wherein the nucleic acid sample is a chromosome